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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|------------------------|-------------|----------------------|---------------------|------------------|
| 10/676,358 | 10/02/2003 | Karinc Vidal | 88265-6852 | 8288 |
| 29157 | 7590 | 03/31/2006 | | EXAMINER |
| BELL, BOYD & LLOYD LLC | | | | KAM, CHIH MIN |
| P. O. BOX 1135 | | | | |
| CHICAGO, IL 60690-1135 | | | ART UNIT | PAPER NUMBER |
| | | | 1656 | |

DATE MAILED: 03/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|------------------------|---------------------|--|
| Office Action Summary | Application No. | Applicant(s) | |
| | 10/676,358 | VIDAL ET AL. | |
| | Examiner | Art Unit | |
| | Chih-Min Kam | 1656 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 03 February 2006.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1 and 3-19 is/are pending in the application.
- 4a) Of the above claim(s) 12-16 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1,3-11 and 17-19 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on 28 July 2005 is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) Notice of References Cited (PTO-892)
- 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.

- 4) Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) Notice of Informal Patent Application (PTO-152)
- 6) Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 1 and 3-19 are pending.

Applicants' amendment filed February 3, 2006 is acknowledged. Applicant's response has been fully considered. Claims 1, 8, 17 and 18 have been amended, and a new claim 19 has been added. Claims 12-16 are non-elected inventions and withdrawn from consideration. Therefore, claims 1, 3-11, and 17-19 are examined.

Withdrawn Informalities

2. The previous objection to the specification (paragraphs 7-9 in the office Action dated July 28, 2005) is withdrawn in view of applicants' amendment to the specification, and applicant's response at page 6 in the amendment filed February 3, 2006.

Withdrawn Claim Rejections - 35 USC § 101

3. The previous rejection to claims 1, 3-7, 11 and 17 under 35 U.S.C. 101 is withdrawn in view of applicants' amendment to the claim, and applicant's response at page 6 in the amendment filed May February 3, 2006.

Withdrawn Claim Rejections - 35 USC § 112

4. The previous rejection to claims 8-10 and 18 under 35 U.S.C. 112, second paragraph, is withdrawn in view of applicants' amendment to the claim, and applicant's response at page 7 in the amendment filed May February 3, 2006.

Withdrawn Claim Rejections - 35 USC § 102

5. The previous rejection of claims 1, 4-7 and 11 under 35 U.S.C. 102(b) as being anticipated by D'Ostilio *et al.* (Clinical and Experimental Immunology 104, 543-546 (June

1996)), is withdrawn in view of applicants' amendment to the claim, and applicant's response at pages 7-8 in the amendment filed February 3, 2006.

Withdrawn Claim Rejections - 35 USC § 102/103

6. The previous rejection of claim 3 under 35 U.S.C. 102(b) as being anticipated by D'Ostilio *et al.* (Clinical and Experimental Immunology 104, 543-546 (June 1996)), or, in the alternative, under 35 U.S.C. 103(a) as obvious over D'Ostilio *et al.* and Simonet *et al.* (WO 99/53942) is withdrawn in view of applicants' amendment to the claim, and applicant's response at page 8 in the amendment filed February 3, 2006.

Maintained Objection to the Specification

7. The specification cites "The OPG of the present invention, i.e. in a form obtainable from milk source, has a polypeptide sequence as identified by SEQ ID. No. 1 and exhibits sizes of about 80, 130 and 200 kDa, respectively, which differs from that obtained by recombinant means (i.e., 55 kDa)." at page 5, lines 8-10 (see also page 12, lines 11-13). However, Fig. 2, the Western blot analysis of human milk fractions under reduced conditions using 10% SDS-gel (page 9, lines 19-25), only shows the band of 130 kDa for various milk fractions containing OPG, it does not show the bands of 80 and 200 kDa for these milk fractions, nor indicates the band of 55 kDa for recombinant OPG. Appropriate clarification is required. Applicants did not respond to the objection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Previous rejection of claims 1 and 3-11 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained, and claim 19 is added to the rejection. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1, 3-11 and 19 are directed to osteoprotegerin isolated from human or bovine milk or colostrums, or obtained from recombination methods in cells, wherein the osteoprotegerin includes a glycosylation pattern giving rise to a polypeptide having a molecular weight of approximately 80, 130 and 200 kDa (claims 1, 3 and 19); a food material, an enteral composition or a pharmaceutical composition comprising the osteoprotegerin (claims 4-7 and 11); or a method of making a food material, an enteral composition or a pharmaceutical composition by adding the osteoprotegerin (claims 8-10). While the specification cites the OPG of the present invention, i.e. in a form obtainable from milk source, has a polypeptide sequence as identified by SEQ ID NO: 1 and exhibits sizes of about 80, 130 and 200 kDa, respectively, which differs from that (i.e., 55 kDa) obtained by recombinant means (see page 5, lines 8-10; page 12, lines 11-13); and the OPG of the present invention may be isolated from milk sources or prepared by recombinant means (page 8, lines 3-8), the specification does not show the OPG obtained from various milk fractions or by recombinant means has a molecular weight of about 80, 130 and 200 kDa (see the bands in Fig. 2). The specification only shows a band of molecular weight of about 130 kDa for various milk fractions and recombinant OPG, and there is no 55 kDa band for recombinant OPG in the western blot (Fig. 2). The lack of description for the osteoprotegerin isolated from human or bovine milk or colostrums, or obtained by recombinant means and

having a glycosylation pattern giving rise to a polypeptide having a molecular weight of approximately 80, 130 and 200 kDa as encompassed by the claims, applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise terms that a skilled artisan would not recognize applicants were in possession of the claimed invention.

Response to Arguments

Applicants indicate the specification states that the OPG of the present invention may be obtained from a milk source, derived from a mammal, in particular from human or bovine milk or colostrum. Human milk OPG has an amino acid sequence of 380 aa and exhibits a molecular weight of approximately 80, 130 and 200 kda when compared to protein markers which were used as molecular weight standards (e.g. BioRad). Applicants provide further details regarding the detected bands in the Western Blot Analysis (see page 12, lines 10-13). Because these claimed elements are sufficiently described in the specification, one having ordinary skill in the art would understand that Applicants had possession of the claimed subject matter even without additional figures (pages 6-7 of the response).

Applicants' response has been fully considered, however, the arguments are not found persuasive because although the specification indicates the milk bands in the Western Blot Analysis were detected at approximately 80, 130 and 200 kDa (see page 5, lines 8-10; page 12, lines 10-13), Fig. 2 only shows 130 kDa band for various milk fractions and recombinant OPG in the Western blot analysis, there are no other bands indicated. Therefore, applicants have failed to sufficiently describe the claimed invention, that is the osteoprotegerin includes a glycosylation pattern giving rise to a polypeptide having a molecular weight of approximately 80, 130 and 200 kDa.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –
(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claim 17 remains rejected under 35 U.S.C. 102(b) as being anticipated by D'Ostilio *et al.* (Clinical and Experimental Immunology 104, 543-546 (June 1996)) as evidenced by US 2004/0137074.

D'Ostilio *et al.* teach human breast milk samples were obtained from eight healthy mothers, and milk samples were collected on days 1-6 post-partum and 1 month after delivery. (page 543, right column). Since the reference teaches using the same source (i.e., human breast milk from healthy mothers; claim 17) for naturally occurring osteoprotegerin as the instant application (see US 2004/0137074, paragraph [0048]), it would be expected that human breast milk (a food material) in the reference inherently contains the same compound as the instant application. Furthermore, since the claim recites the term “a food material containing an osteoprotgerin isolated from human milk”, it would be expected that the human breast milk in the reference has the same composition as the claimed invention, the isolation step does not change the composition of the claim.

10. Claim 18 is rejected under 35 U.S.C. 102(b) as being anticipated by Boyle *et al.* (U.S. Patent 6,015,938, January 18, 2000).

Boyle *et al.* teach an osteoprotegerin (OPG) obtained by expressing in host cells is useful for treating bone disease (column 2, lines 23-53), and a pharmaceutical composition comprising

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a therapeutically effective amount of OPG together with a pharmaceutically acceptable diluent, carrier, solubilizer, emulsifier, preservative and/or adjuvant, the composition may be in a liquid or lyophilized form (column 9, lines 20-45; claim 18). Although claim 18 recites osteoprotegerin isolated from human or bovine milk, the claimed osteoprotegerin is not different from the osteoprotegerin in the reference since there is no characteristic of the protein indicated in the claim. Since the pharmaceutical composition of Boyle *et al.* contains a therapeutically effective amount of OPG, it would be expected that the amount of OPG is effective to assist in formation of lymphoid tissues and regulation of immune responses in a subject, which meet the criteria of the claimed pharmaceutical composition.

Conclusion

11. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached at 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chih-Min Kam, Ph. D.
Patent Examiner



CHIH-MIN KAM
PATENT EXAMINER

CMK

March 24, 2006